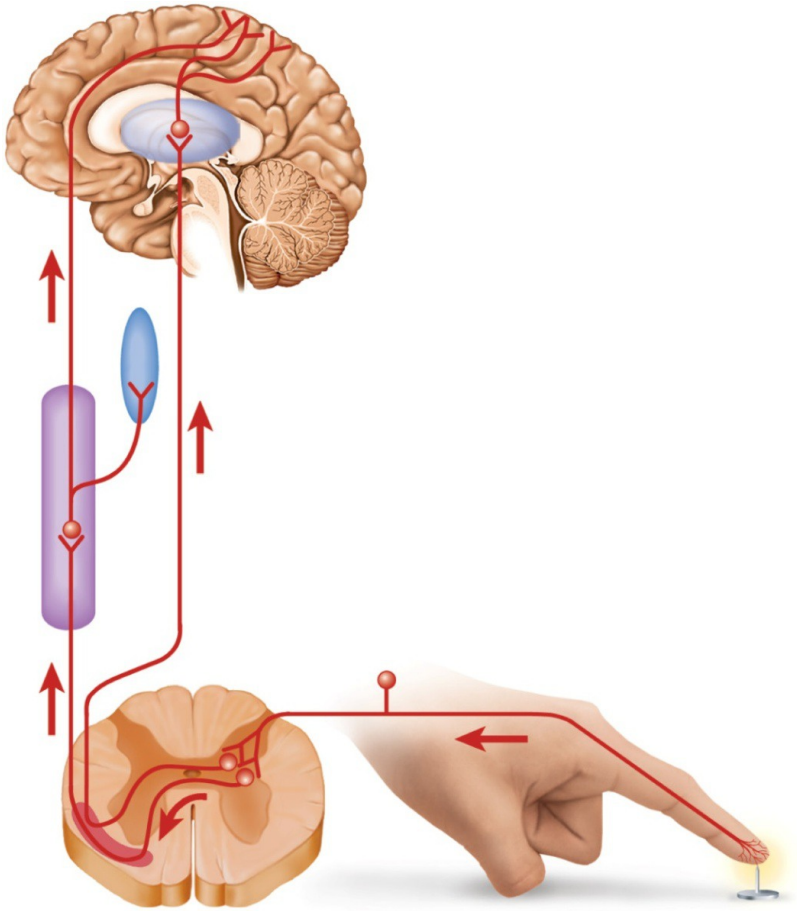
Chapter 16.4

The Sense of Pain



Pain

- Pain is discomfort caused by tissue injury or noxious stimulation that typically leads to evasive action
  - pain tells us something is wrong! (This is beneficial)
  - protect us from sustaining more tissue damage
  - lost of pain in diabetes mellitus = **diabetic neuropathy**
  - if you lose sense of pain then you can not detect tissue damage (e.g. Leprosy)
- **Nociceptors** = pain receptors (unencapsulated dendrites)
  - two types providing different pain sensations
  - **fast pain (alpha)** travels in myelinated fibers at 12 - 30 m/sec /// sharp, localized, stabbing pain perceived with injury
  - **slow pain (delta)** travels unmyelinated fibers at 0.5 - 2 m/sec /// longer-lasting, dull, diffuse feeling
  - Both type in skin // damage to skin first detect by alpha fibers followed by delta fibers

Pain

- **somatic pain** - from skin, muscles and joints

- **visceral pain** - from the viscera - stretch, chemical irritants or ischemia of viscera (poorly localized)

- injured tissues release chemicals that stimulate pain fibers /// **bradykinin** - most potent pain stimulus known

  - makes us aware of injury and activates cascade or reactions that promote healing

  - *histamine, prostaglandin, potassium ions, ATP, and serotonin* are molecules that also stimulate nociceptors

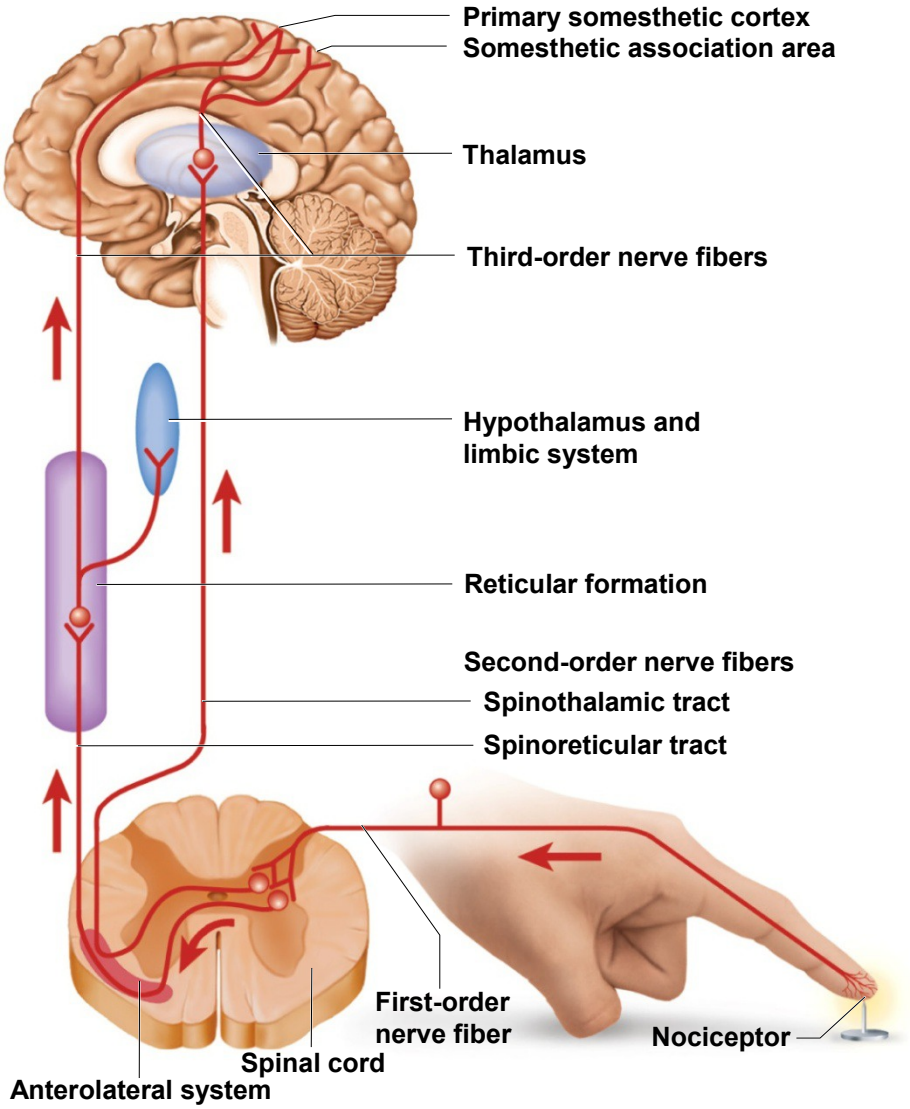
Projection Pathway for Pain

- Ascending and descending tracts (plus multiple sub-routes)
- Ascending pain neurons route to somatic sensory gyrus:
    - **first-order neuron** cell bodies in dorsal root ganglion of spinal nerves or cranial nerves V, VII, IX, and X
    - **second-order neurons** decussate and send fibers up spinothalamic tract (somatic pain) or through medulla to thalamus /// 2nd order gracile fasciculus carries visceral pain signals
    - **third-order neurons** from thalamus reach postcentral gyrus of cerebrum (somatic sensory gyrus)

Projection Pathway for Pain

- Pain signals four ascending tracts:
  - **spinothalamic tract** – most significant pain pathway /// carries most somatic pain signals
  - **spinoreticular tract** – carries pain signals to reticular formation /// activate visceral, emotional and behavioral reactions to pain
  - **gracile fasciculus** – carries signals to the thalamus for visceral pain -- lower extremities
  - **cuniate fasiculus** – carries signals to the thalamus for visceral pain -- upper extremities

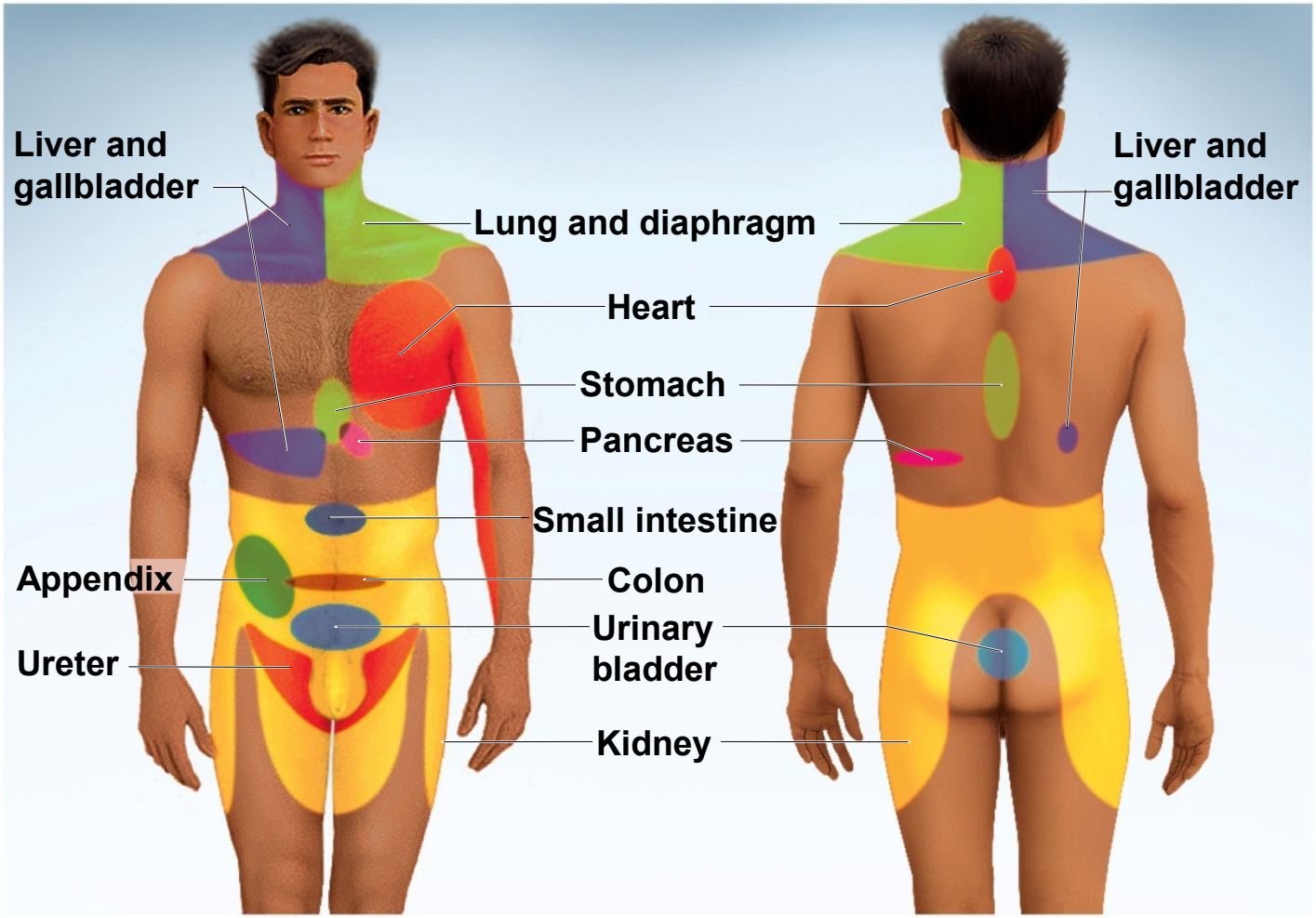
Pain Signal Destinations



Referred Pain

- Pain originates in deep viscera is sensed as coming from the skin or another superficial site
  - results from convergence of neural pathways in CNS
  - brain “assumes” visceral pain is coming from skin /// brain can not distinguish true source of pain
  - pain originating in heart pain felt in shoulder or arm because both send pain input to spinal cord segments T1 to T5

Referred Pain



CNS Modulation of Pain

- Analgesic = pain-relieving // target mechanisms in CNS /// just beginning to be understood
  - tied to receptor sites located in the brain for drugs like opium, morphine & heroin
  - enkephalins – analgesic oligopeptides with 200 times the potency of morphine /// made naturally by our bodies (e.g.)
    - endorphins
    - dynorphins
    - other larger analgesic neuropeptides have been discovered

CNS Modulation of Pain

- endogenous opioids /// internally produced opium-like substances
  - enkephalins, endorphins, and dynorphins
  - secreted by the CNS, pituitary gland, digestive tract, and other organs
- neuromodulators
  - enkephalins can block the transmission of pain signals
  -
- opiods also produce feelings of pleasure and euphoria

Where Does Spinal Gating Occur?

- Stops pain signals at the posterior horn of the spinal cord
  - descending analgesic fibers arise in brain stem's reticular formation
  - travel down the spinal cord in the reticulospinal tract
  - block pain signals from traveling up the cord to the brain

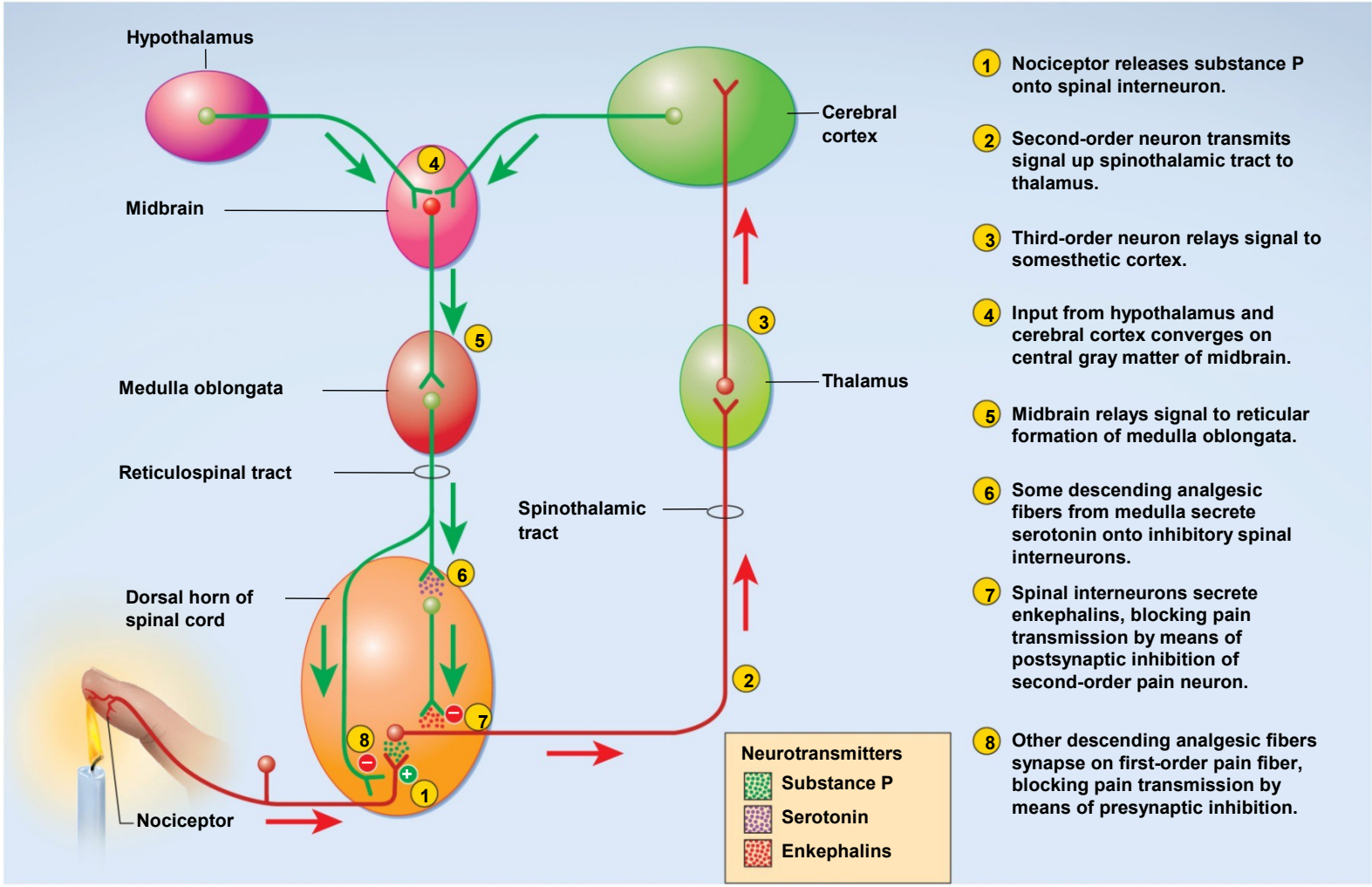
Spinal Gating

- Normal pain pathway (ascending)
  - **nociceptor** stimulates second-order nerve fiber
  - **substance P** is neurotransmitter at this synapse
  - second-order fiber transmits signal up the **spinothalamic tract** to the thalamus
  - **thalamus** relays the signals through third order neurons to the cerebral cortex where one becomes conscious of the pain

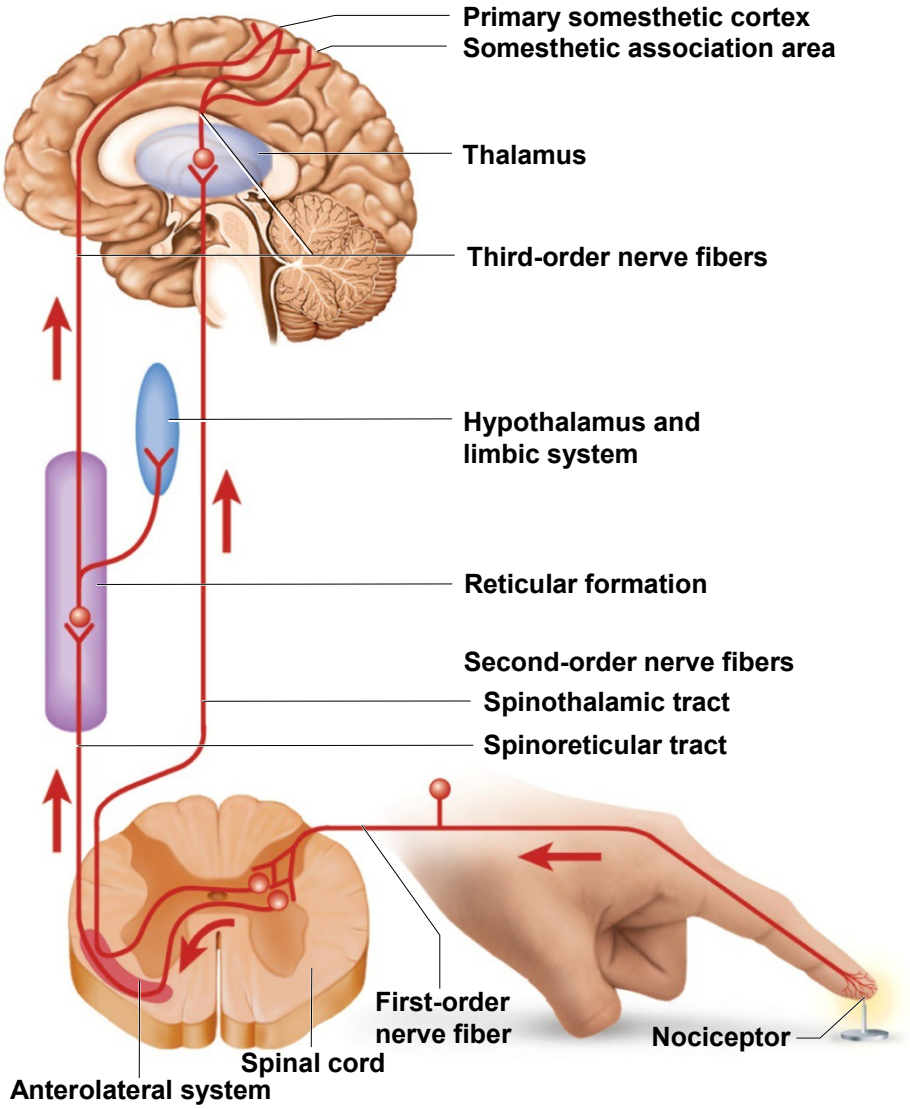
Spinal Gating: Pathway for Pain Blocking

- signals from the hypothalamus and cerebral cortex feed into the central gray matter of the midbrain // allows both autonomic and conscious influences on pain perception
- midbrain relays signals to certain nuclei in the reticular formation of the medulla oblongata
- medulla issues descending, serotonin-secreting analgesic fibers to the spinal cord // terminate in the posterior horn at all levels of the spinal cord
- in posterior horn, descending analgesic fibers synapse on short spinal interneurons (i.e. local circuit neurons)
- the interneurons synapse on the second-order pain fiber // secrete enkephalins to inhibit the second-order neuron
- some fibers from the medulla also exert presynaptic inhibition by synapsing on the axons of nociceptors and blocking the release of substance P

Spinal Gating of Pain Signals



Pain Signal Destinations (Ascending)



How to Interrupt Spinal Gating

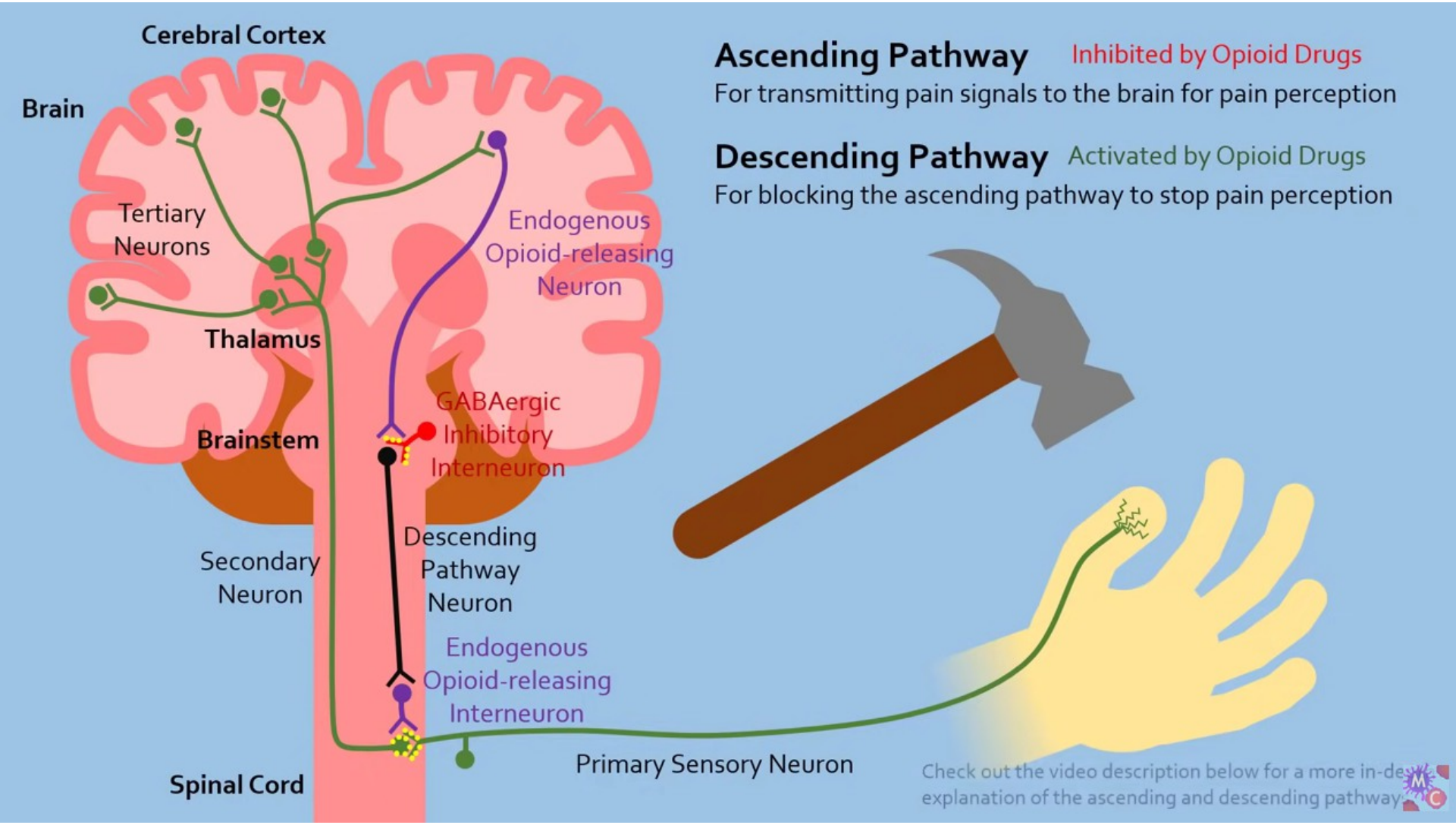
Rubbing or massaging injury

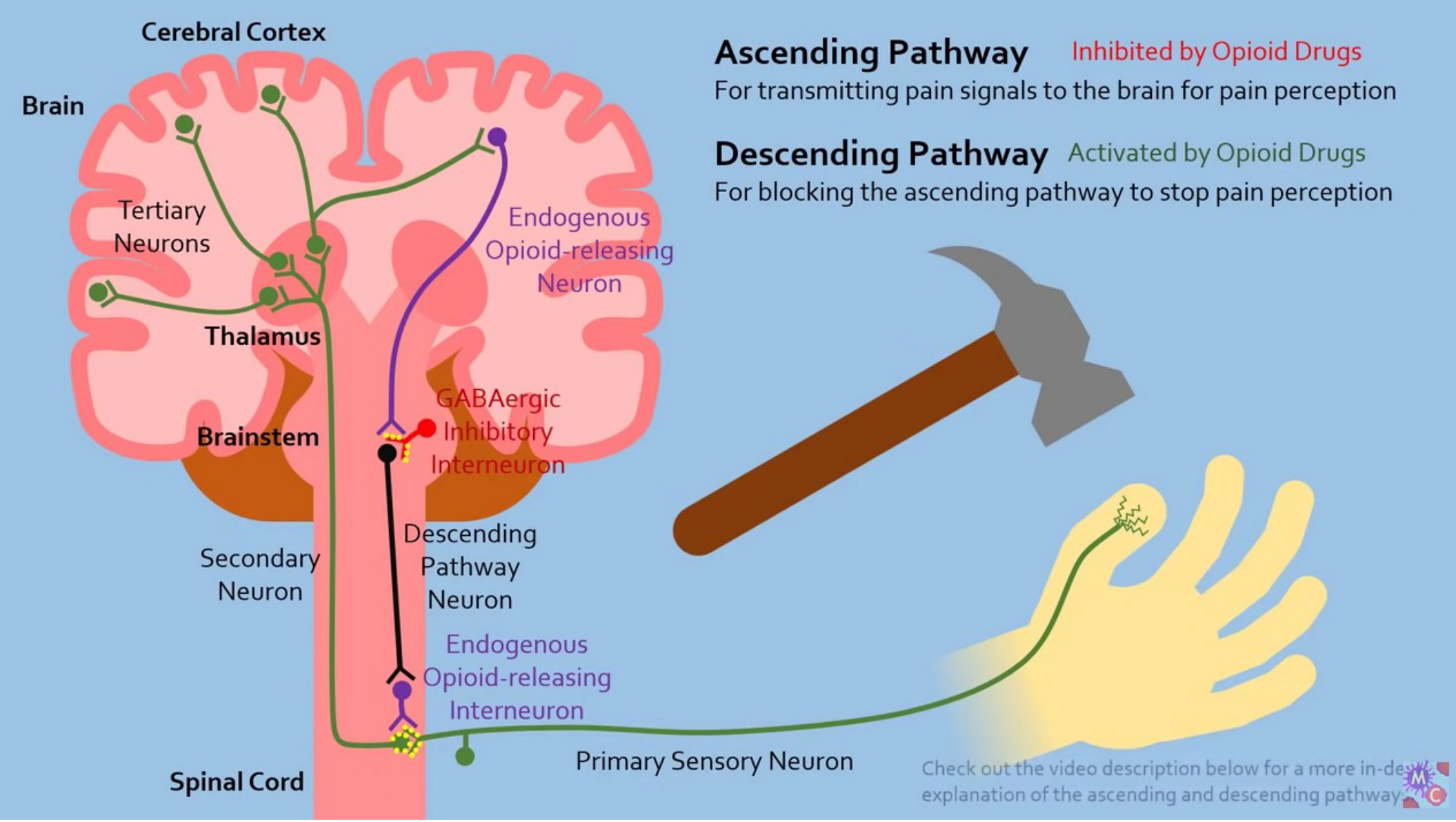
another pathway to initiate spinal gating

pain-inhibiting neurons of the posterior horn receive input from mechanoreceptors in the skin and deeper tissues

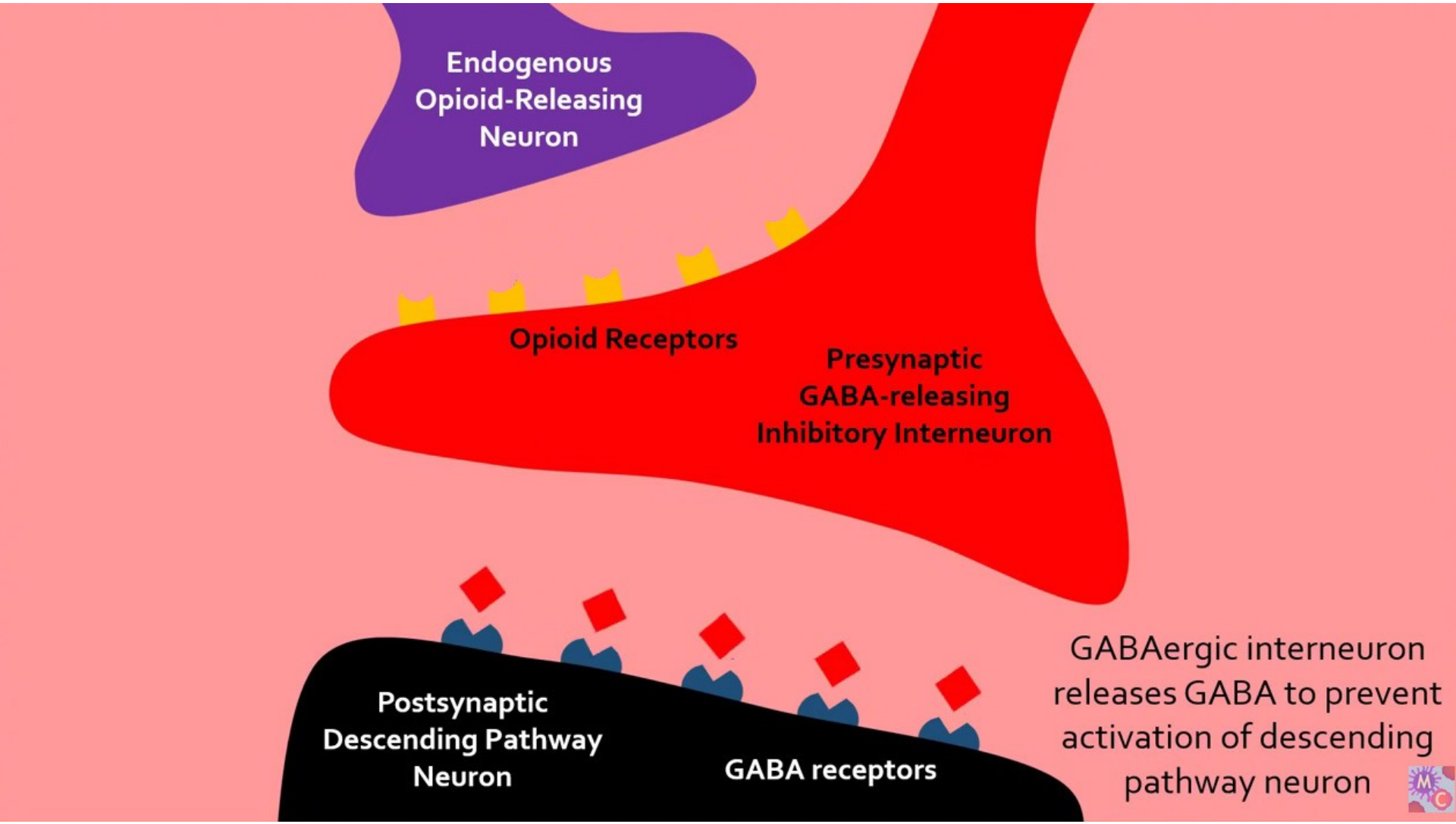
rubbing stimulates mechanoreceptors which stimulates spinal interneurons to secrete enkephalins that inhibit second-order pain neurons

How Opioids Block Pain

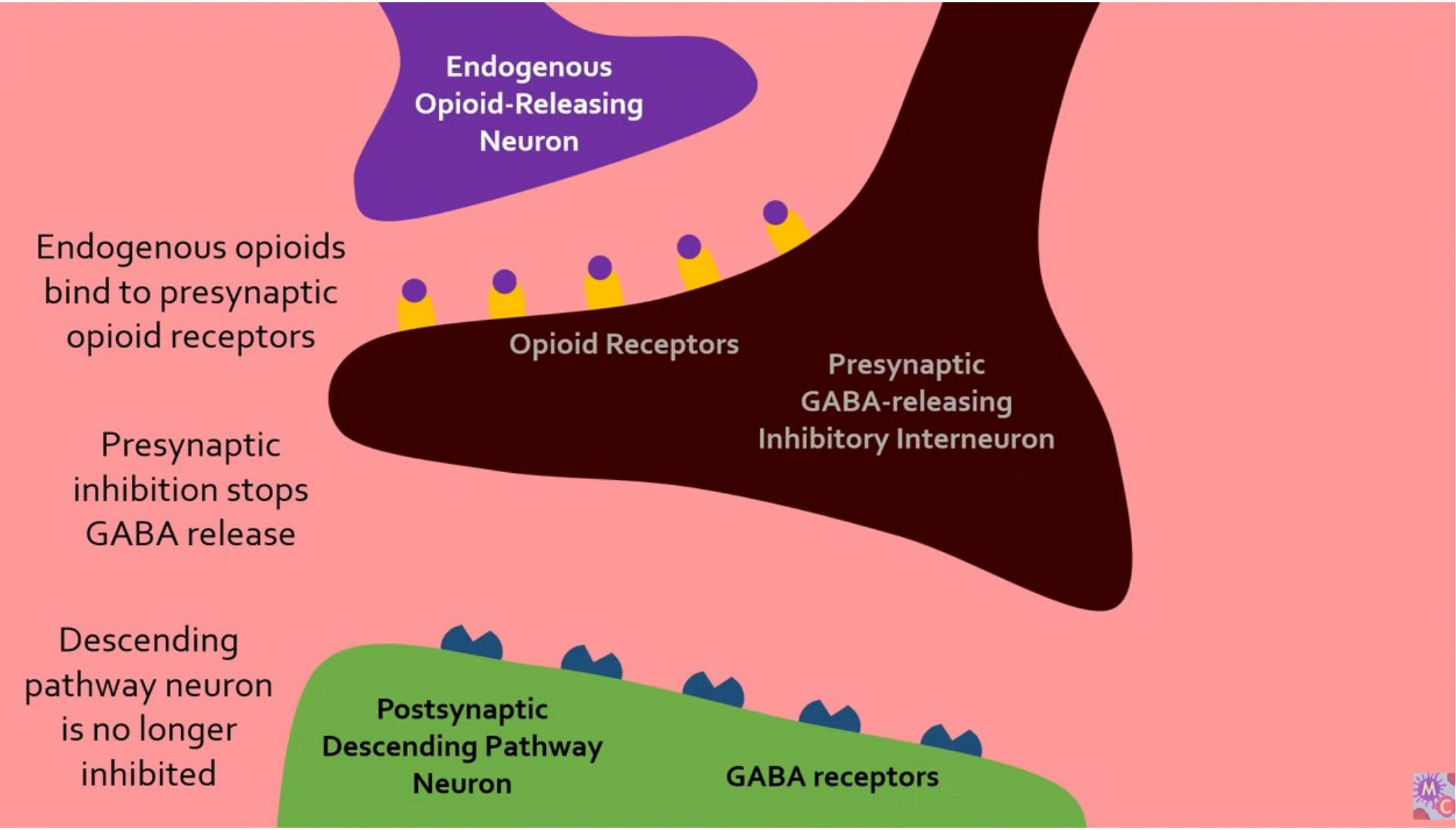




If ascending pain signals is not blocked by descending pathway then the brain will know the location of pain, degree of pain, and decide if pain is great enough to block ascending pain signal. Releasing endogenous opioids in the brainstem removes inhibition and descending pathway signal moves to dorsal horn.

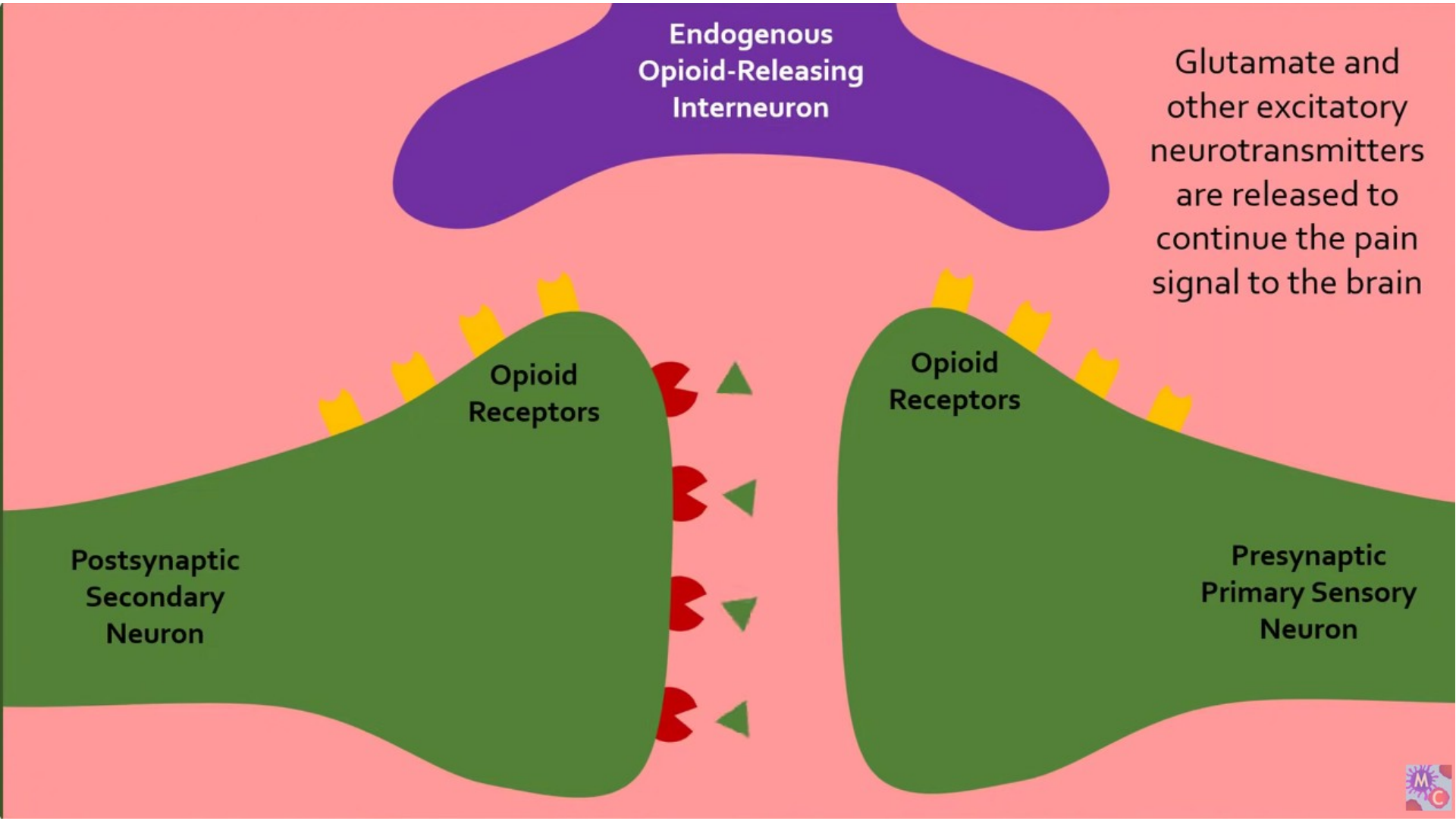


Ascending pain signals not blocked by descending pathway. If there is enough pain then brain will know the location of pain, degree of pain, and may now release endogenous opioids to send signal down descending pathway and stop pain signal.

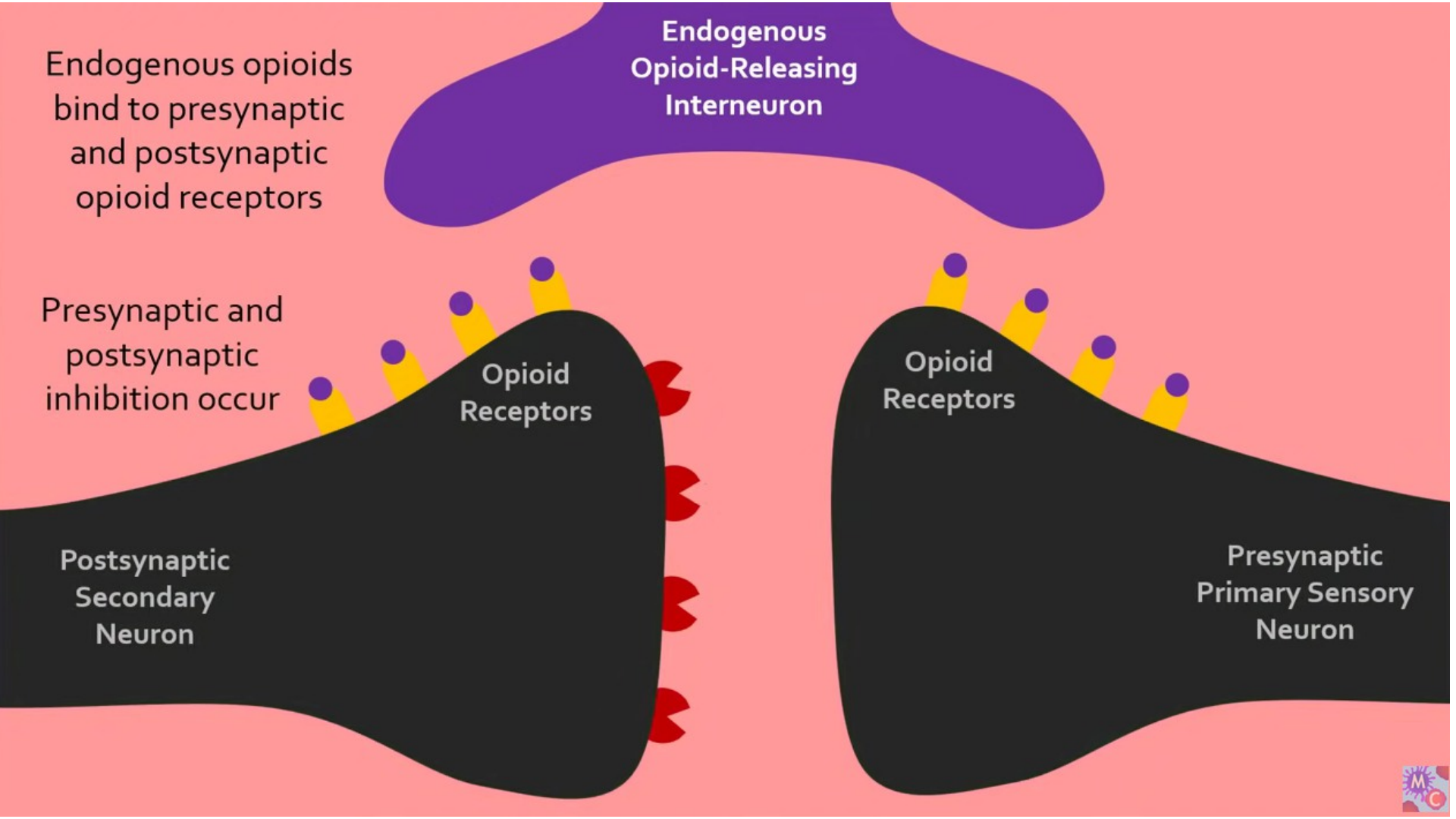


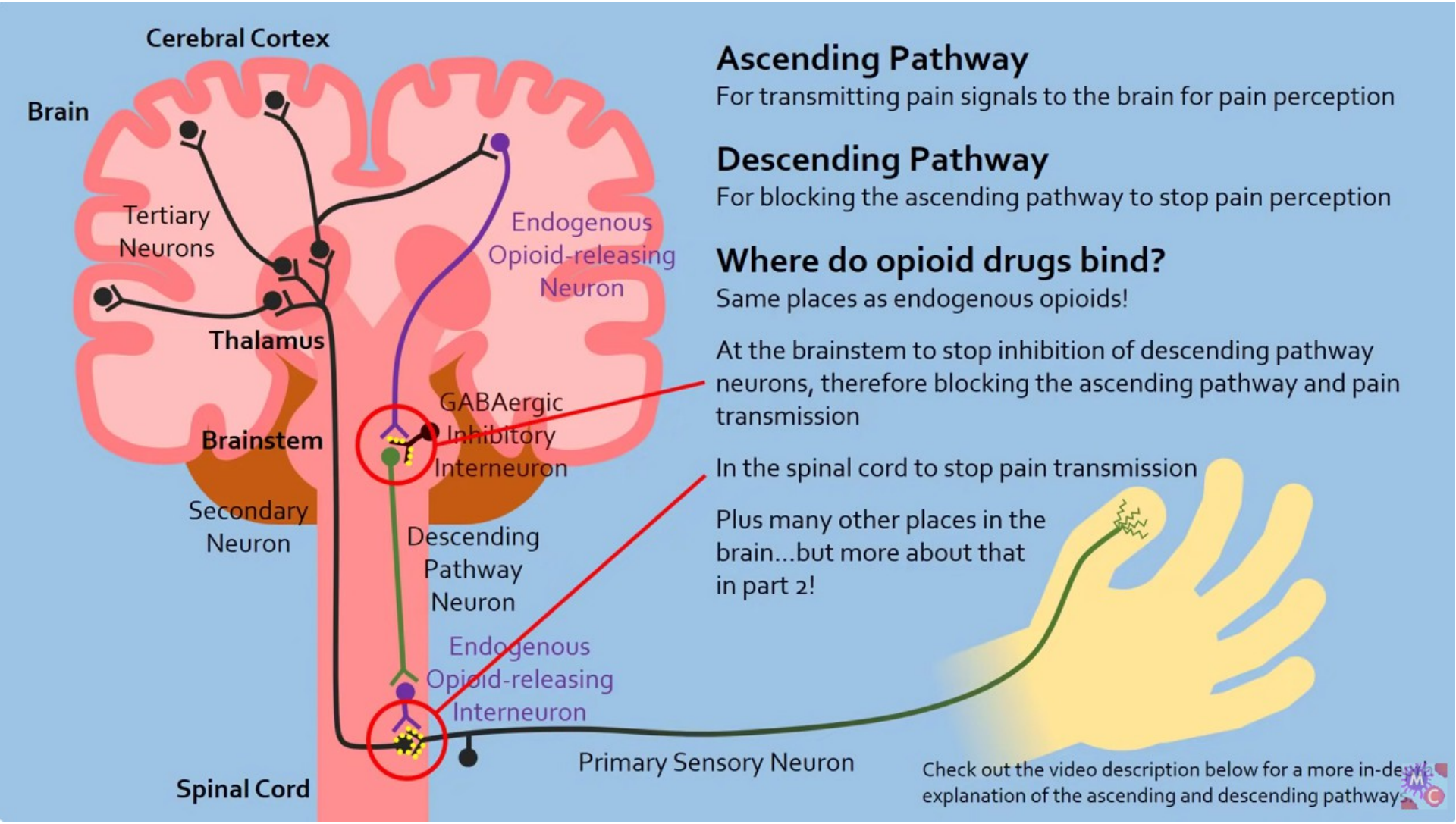
Endogenous opioids block voltage regulated calcium gates to prevent exocytosis of GABA.

This is what occurs if descending pathway is blocked by GABA.



If GABA is blocked then descending signal is not inhibited and descending neuron releases endogenous opioid which blocks ascending pain signal.




Cerebral Cortex
Brain
Tertiary Neurons
Endogenous Opioid-releasing Neuron
Thalamus
GABAergic Inhibitory Interneuron
Brainstem
Secondary Neuron
Descending Pathway Neuron
Endogenous Opioid-releasing Interneuron
Primary Sensory Neuron
Spinal Cord
Ascending Pathway
For transmitting pain signals to the brain for pain perception
Descending Pathway
For blocking the ascending pathway to stop pain perception
Where do opioid drugs bind?
Same places as endogenous opioids!
At the brainstem to stop inhibition of descending pathway neurons, therefore blocking the ascending pathway and pain transmission
In the spinal cord to stop pain transmission
Plus many other places in the brain...but more about that in part 2!
Check out the video description below for a more in-de
explanation of the ascending and descending pathways